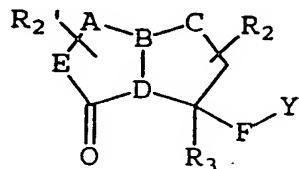


Claims

What is claimed is:

1. A method for inhibiting a protease, comprising administering to an animal in need thereof an effective amount of a compound having the structure:



and pharmaceutically acceptable salts thereof,  
wherein

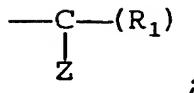
A is selected from  $-C(=O)-$ ,  $-(CH_2)_{0-4}-$ ,  $-C(=O)(CH_2)_{1-3}-$ ,  $-(CH_2)_{1-2}O-$  and  $-(CH_2)_{1-2}S-$ ;

B is selected from N and CH;

C is selected from  $-C(=O)-$ ,  $-C(=O)(CH_2)_{1-3}-$ ,  $-(CH_2)_{0-3}-$ ,  $-O-$ ,  $-S-$ ,  $-O-(CH_2)_{1-2}-$  and  $-S(CH_2)_{1-2}-$ ;

D is selected from N and C( $R_4$ );

E is selected from  $\begin{array}{c} -C(R_1)- \\ | \\ NHZ \end{array}$ ,  $\begin{array}{c} —N— \\ | \\ Z \end{array}$  and



; F is an optional carbonyl moiety;

$R_1$  and  $R_4$  are independently selected from amino acid side chain moieties and derivatives thereof;

$R_2$  and  $R_2'$  represent one or more ring substituents individually selected from an amino acid side chain moiety and derivatives thereof, or  $R_2$  taken

together with C or Y forms a fused substituted or unsubstituted homocyclic or heterocyclic ring;

R, is selected from an amino acid side chain moiety and derivatives thereof, or taken together with C forms a bridging moiety selected from -(CH<sub>2</sub>)<sub>1-2</sub>-, -O- and -S-;

Y and Z represent the remainder of the molecule; and

any two adjacent CH groups of the bicyclic ring may form a double bond.

2. The method of claim 1 wherein E is  $\begin{array}{c} -C(R_1)- \\ | \\ NHZ \end{array}$

3. The method of claim 1 wherein E is  $\begin{array}{c} —N— \\ | \\ Z \end{array}$

4. The method of claim 1 wherein E is  $\begin{array}{c} —C—(R_1) \\ | \\ Z \end{array}$ ,  
with the proviso that Z does not contain an -NH- moiety attached to the carbon atom bearing the R<sub>1</sub> substituent.

5. The method of claim 1 wherein the protease is a serine protease.

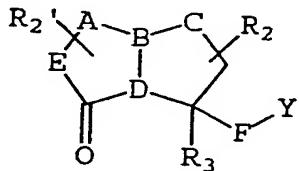
6. The method of claim 5 wherein the serine protease is selected from thrombin, Factor X, Factor IX, Factor VII, Factor XI, urokinase, HCV protease, chymase, trypsin and kallikrein.

7. The method of claim 5 wherein the serine protease is thrombin.

8. The method of claim 5 wherein the serine protease is Factor VII

9. The method of claim 1 wherein the protease is selected from an aspartic, cysteine and metallo protease.

10. A method for inhibiting a kinase, comprising administering to an animal in need thereof an effective amount of a compound having the structure:



and pharmaceutically acceptable salts thereof,

wherein

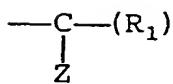
A is selected from  $-C(=O)-$ ,  $-(CH_2)_{0-4}-$ ,  $-C(=O)(CH_2)_{1-3}-$ ,  $-(CH_2)_{1-2}O-$  and  $-(CH_2)_{1-2}S-$ ;

B is selected from N and CH;

C is selected from  $-C(=O)-$ ,  $-C(=O)(CH_2)_{1-3}-$ ,  $-(CH_2)_{0-3}-$ ,  $-O-$ ,  $-S-$ ,  $-O-(CH_2)_{1-2}-$  and  $-S(CH_2)_{1-2}-$ ;

D is selected from N and C( $R_4$ );

E is selected from  $\begin{array}{c} -C(R_1)- \\ | \\ NHZ \end{array}$ ,  $\begin{array}{c} —N— \\ | \\ Z \end{array}$  and



F is an optional carbonyl moiety;

$R_1$  and  $R_4$  are independently selected from amino acid side chain moieties and derivatives thereof;

$R_2$  and  $R_2'$  represent one or more ring substituents individually selected from an amino acid side chain moiety and derivatives thereof, or  $R_2$  taken together with C or Y forms a fused substituted or unsubstituted homocyclic or heterocyclic ring;

$R_3$  is selected from an amino acid side chain moiety and derivatives thereof, or taken together with C forms a bridging moiety selected from  $-(CH_2)_{1-2}-$ , -O- and -S-;

Y and Z represent the remainder of the molecule; and

any two adjacent CH groups of the bicyclic ring may form a double bond.

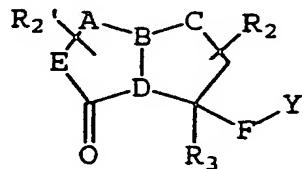
11. The method of claim 10 wherein E is  $\begin{array}{c} -C(R_1)- \\ | \\ NHZ \end{array}$ .

12. The method of claim 10 wherein E is  $\begin{array}{c} —N— \\ | \\ Z \end{array}$ .

13. The method of claim 10 wherein E is  $\begin{array}{c} —C—(R_1) \\ | \\ Z \end{array}$ ,  
with the proviso that Z does not contain an -NH- moiety attached to the carbon atom bearing the  $R_1$  substituent.

14. The method of claims 10 wherein the kinase is a serine/threonine or tyrosine kinase.

15. A method for inhibiting a transcription factor, comprising administering to an animal in need thereof an effective amount of a compound having the structure:



and pharmaceutically acceptable salts thereof,

wherein

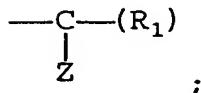
A is selected from  $-C(=O)-$ ,  $-(CH_2)_{0-4}-$ ,  $-C(=O)(CH_2)_{1-3}-$ ,  $-(CH_2)_{1-2}O-$  and  $-(CH_2)_{1-2}S-$ ;

B is selected from N and CH;

C is selected from  $-C(=O)-$ ,  $-C(=O)(CH_2)_{1-3}-$ ,  $-(CH_2)_{0-3}-$ ,  $-O-$ ,  $-S-$ ,  $-O-(CH_2)_{1-2}-$  and  $-S(CH_2)_{1-2}-$ ;

D is selected from N and C( $R_4$ ) ;

E is selected from  $\begin{array}{c} -C(R_1)- \\ | \\ NHZ \end{array}$ ,  $\begin{array}{c} ---N--- \\ | \\ Z \end{array}$  and



; F is an optional carbonyl moiety;

$R_1$  and  $R_4$  are independently selected from amino acid side chain moieties and derivatives thereof;

$R_2$  and  $R_2'$  represent one or more ring substituents individually selected from an amino acid side chain moiety and derivatives thereof, or  $R_2$  taken together with C or Y forms a fused substituted or unsubstituted homocyclic or heterocyclic ring;

$R_3$  is selected from an amino acid side chain moiety and derivatives thereof, or taken together with C

forms a bridging moiety selected from  $-(CH_2)_{1-2}-$ ,  $-O-$  and  $-S-$ ;

Y and Z represent the remainder of the molecule; and

any two adjacent CH groups of the bicyclic ring may form a double bond.

16. The method of claim 15 wherein E is  $\begin{array}{c} -C(R_1)- \\ | \\ NHZ \end{array}$

17. The method of claim 15 wherein E is  $\begin{array}{c} ---N--- \\ | \\ Z \end{array}$

18. The method of claim 15 wherein E is  $\begin{array}{c} ---C---(R_1) \\ | \\ Z \end{array}$ ,

with the proviso that Z does not contain an  $-NH-$  moiety attached to the carbon atom bearing the R<sub>1</sub> substituent.

19. The method of claim 15 wherein the ability of the transcription factor to bind DNA is controlled by reduction of a cysteine residue by a cellular oxidoreductase.

20. The method of claim 15 wherein the transcription factor is selected from NF- $\kappa$ B, AP-1, Myb, GRE, STAT-1 through -6, NFAT, IRF-1 and MAF.

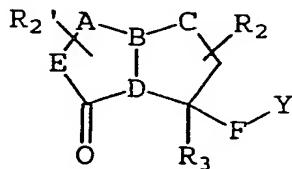
21. The method of claim 15 wherein the transcription factor is NF- $\kappa$ B.

22. The method of claim 15 wherein the transcription factor is AP-1.

23. The method of claim 19 wherein the cellular oxidoreductase is ref-1.

24. The method of claim 15 wherein the warm-blooded animal has been diagnosed with, or is at risk of developing, a condition selected from Crohn's disease, asthma, rheumatoid arthritis, ischemia-reperfusion injury, GVHD, ALS, Alzheimer's disease, allograft rejection, adult T-cell leukemia, cancer and inflammatory bowel disease.

25. A method for inhibiting protein-protein binding interactions, comprising administering to an animal in need thereof an effective amount of a compound having the structure:



and pharmaceutically acceptable salts thereof,

wherein

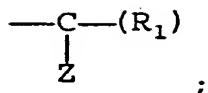
A is selected from  $-C(=O)-$ ,  $-(CH_2)_{0-4}-$ ,  $-C(=O)(CH_2)_{1-3}-$ ,  $-(CH_2)_{1-2}O-$  and  $-(CH_2)_{1-2}S-$ ;

B is selected from N and CH;

C is selected from  $-C(=O)-$ ,  $-C(=O)(CH_2)_{1-3}-$ ,  $-(CH_2)_{0-3}-$ ,  $-O-$ ,  $-S-$ ,  $-O-(CH_2)_{1-2}-$  and  $-S(CH_2)_{1-2}-$ ;

D is selected from N and C( $R_4$ );

E is selected from  $\begin{array}{c} -C(R_1)- \\ | \\ NHZ \end{array}$ ,  $\begin{array}{c} -N- \\ | \\ Z \end{array}$  and



F is an optional carbonyl moiety;

R<sub>1</sub> and R<sub>4</sub> are independently selected from amino acid side chain moieties and derivatives thereof;

R<sub>2</sub> and R<sub>2'</sub> represent one or more ring substituents individually selected from an amino acid side chain moiety and derivatives thereof, or R<sub>2</sub> taken together with C or Y forms a fused substituted or unsubstituted homocyclic or heterocyclic ring;

R<sub>3</sub> is selected from an amino acid side chain moiety and derivatives thereof, or taken together with C forms a bridging moiety selected from -(CH<sub>2</sub>)<sub>1-2</sub>-, -O- and -S-;

Y and Z represent the remainder of the molecule; and

any two adjacent CH groups of the bicyclic ring may form a double bond.

26. The method of claim 25 wherein E is  $\begin{array}{c} -C(R_1)- \\ | \\ NHZ \end{array}$ .

27. The method of claim 25 wherein E is  $\begin{array}{c} -N- \\ | \\ Z \end{array}$ .

28. The method of claim 25 wherein E is  $\begin{array}{c} -C-(R_1) \\ | \\ Z \end{array}$ , with the proviso that Z does not contain an -NH- moiety attached to the carbon atom bearing the R<sub>1</sub> substituent.

29. The method of claim 25 wherein the protein-protein binding interaction is between the SH2 domain or the PDZ domain and another protein.